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Changes in Spontaneous Sinus Node Rate as an Estimate of Cardiac Autonomic Tone During Stable and Unstable Ventricular Tachycardia

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Changes in sinus node rate were measured as an estimate of reflex control of cardiac autonomic tone during 32 episodes of stable ventricular tachycardia (without loss of consciousness) and 21 episodes of unstable ventricular tachycardia (loss of consciousness requiring electrical cardioversion) in 32 patients without retrograde ventriculoatrial conduction. Sinus node rate was measured before induction of ventricular tachycardia (at 5 s intervals during tachycardia) and 5 s after termination of ventricular tachycardia. It increased from 85 ± 12 beats/min to a maximum of 109 ± 25 beats/min during stable ventricular tachycardia ($p < 0.001$) and from 82 ± 15 beats/min to a maximum of 105 ± 34 beats/min during unstable ventricular tachycardia ($p < 0.001$).

During unstable ventricular tachycardia, the increase in sinus rate was more abrupt and was followed by a sharp decrease beginning before termination of the tachycardia and resulting in a slower rate after termination (56 ± 15 beats/min) than before tachycardia ($p < 0.001$). Stable ventricular tachycardia resulted in a continuous increase of sinus node rate, which remained higher after termination (102 ± 15 beats/min) than before tachycardia ($p < 0.001$). Autonomic mechanisms responsible for changes in sinus rate were evaluated by reinducing the ventricular tachycardia after beta-adrenergic blockade by propranolol in 10 patients. Intravenous propranolol (mean dose 11 ± 4 mg) had no effect on the magnitude of increase in sinus rate (+18 ± 6 beats/min before and +17 ± 7 beats/min after propranolol).

It is concluded that 1) induced ventricular tachycardia is accompanied by an increase in sinus node rate, which is not altered by beta-blockade, suggesting that sympathetic activation is not a predominant mechanism; and 2) changes in sinus node rate are different during stable and unstable ventricular tachycardia. The latter differences may be due to differences in the autonomic reflexes elicited by the two arrhythmias.

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Changes in autonomic tone may modulate the electrophysiologic properties of arrhythmia substrate and influence the hemodynamic stability of ventricular tachycardia (1–4), but little information is available concerning the changes in cardiac neural activity after the onset of ventricular tachycardia in humans (4). Tachycardia itself, by alterations in systemic arterial pressure and cardiac filling pressures, might be expected to produce changes in autonomic tone by altering input from baroreceptors and from cardiac mechanoreceptors.

Because changes in spontaneous sinus node rate reflect the cardiac sympathetic-parasympathetic interactions (5–7), an induced ventricular tachycardia without retrograde ventriculoatrial conduction allows the use of changes in sinus node rate to estimate autonomic tone. In this study, we measured sinus rate during induced ventricular tachycardia and compared changes of sinus rate during tachycardia resulting in either stable or unstable presentation. The role of autonomic mechanisms, implied by changes in sinus rate, was estimated by reinducing the ventricular tachycardia after administration of intravenous propranolol in 10 patients.

Methods

Study patients (Table 1). Thirty-two consecutive patients (29 men and 3 women, mean age 64 ± 10 years) were included in the study. Entry required reproducible inducibil-

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Table 1. Clinical Characteristics of 32 Patients

	Patients With Stable VT (n = 16)	Patients With Unstable VT (n = 16)
Underlying heart disease		
Coronary artery disease	15	13
Previous myocardial infarction	12	9
Cardiomyopathy	1	3
No. of diseased coronary vessels		
One vessel disease	4	1
Two vessel disease	3	6
Three vessel disease	8	6
Location of prior myocardial infarction		
Anterior	6	1
Inferior	4	4
Anterior + inferior	2	4
Indication for EP study		
Cardiac arrest	3	10
Ventricular tachycardia	12	5
Unexplained syncope	1	1
Clinical arrhythmia presentation		
Ventricular tachycardia	12	4
Ventricular fibrillation	2	10
Not known	2	2
Cardiac medication		
Digitalis	3	1
Diuretic	4	4
Calcium channel blocking agent	3	2
Vasodilator	3	2
Nitrate	4	4

EP = electrophysiologic; VT = ventricular tachycardia.

ity of sustained ventricular tachycardia during an electrophysiologic study without retrograde ventriculoatrial conduction and with regular sinus node activity. The clinical presentation was sustained ventricular tachycardia in 17 patients and cardiac arrest in 13, whereas 2 had unexplained syncope. None of the events were associated with myocardial infarction. Patients with clinical findings suggestive of sinus node dysfunction or prolonged sinus node recovery time on electrophysiologic study were excluded. Patients in whom ventricular fibrillation was induced without initial constant cycle length ventricular tachycardia, and those whose stable ventricular tachycardia became unstable after an attempt to terminate the tachycardia by pacing, were excluded.

All patients had had cardiac catheterization with left ventriculography and coronary angiography to document the etiology and extent of cardiac disease. All cardioactive drugs, with the exception of digitalis or other agents used for clinical indications other than arrhythmia, were discontinued at least five elimination half-lives before electrophysiologic studies. No patient was receiving a beta-adrenergic blocker at the time of electrophysiologic studies. All patients provided informed consent for electrophysiologic studies that were performed for clinical indications.

Electrophysiologic studies. Electrophysiologic studies were carried out in the postabsorptive state with mild sedation induced by diazepam. Electrode catheters were introduced percutaneously by way of the femoral veins and positioned in the right atrium, tricuspid valve area and right ventricle. Intracardiac electrograms, filtered at 30 to 500 Hz, were displayed simultaneously with surface electrocardiographic leads I, II and V_1. Recordings were obtained at a paper speed of 100 mm/s with use of a Gould multichannel paper recorder. A custom-designed programmable stimulator was used (Bloom Associates), which provides square pulses 2 ms in duration with variable current strength. Pacing impulses were delivered at twice diastolic threshold.

Pacing and stimulation protocol. After measurement of baseline conduction intervals and completion of the atrial pacing protocol, including measurement of sinus node recovery time, the ventricular pacing protocol was started. The ventricular stimulation protocol consists of 1) incremental ventricular pacing; and 2) programmed ventricular stimulation by delivering single, double and triple extrastimuli during up to two basic drive cycle lengths from one or two right ventricular pacing sites. The end points of this stimulation protocol were: 1) reproducible induction of sustained ventricular tachycardia; or 2) induction of ventricular fibrillation. Attempts to reinduce the ventricular tachycardia were started after a ≥10 to 15 min rest period when the heart rate had returned to baseline level. Stimulation was not usually repeated for reinduction of ventricular fibrillation.

The pacing protocol began with incremental ventricular stimulation from the right ventricular apex at a cycle length 50 ms shorter than sinus cycle length. The pacing cycle length was progressively decreased by 50 ms decrements until a cycle length of 300 ms was reached. If end points were not achieved, programmed ventricular stimulation was performed with a single extrastimulus and then with double and triple extrastimuli if required. The coupling intervals between extrastimuli were changed in 10 to 20 ms decrements. If sustained ventricular tachycardia was not induced by either incremental pacing or the application of single, double or triple extrastimuli with two different basic drive cycle lengths, the identical protocol was repeated from the right ventricular outflow tract. On induction of sustained ventricular tachycardia, the level of consciousness of the patient was monitored, and a countershock was delivered as soon as the patient became unresponsive to verbal stimuli.

Definitions. Stable ventricular tachycardia was defined as monomorphic constant cycle length tachycardia without loss of consciousness. Unstable ventricular tachycardia was a constant cycle length tachycardia resulting in loss of consciousness and requiring electrical cardioversion for termination. Stable tachycardia was terminated by extrastimuli, rapid ventricular pacing or countershock, if needed.

Sinus node rate measurements. Sinus node activity was estimated from a right atrial electrogram recorded by the electrode catheter located in the high right atrium. The sinus rate was measured from three consecutive atrial impulses before ventricular tachycardia, at 5 s intervals until termination of tachycardia and then 5 s after termination of ventricular tachycardia.

Intravenous propranolol. Changes in sinus rate during ventricular tachycardia were measured before and after intravenous propranolol in 10 patients (4 with stable and 6 with unstable induced ventricular tachycardia before propranolol). Intravenous propranolol was given in 1 mg bolus injections until a 15% decrease of sinus rate was achieved. If signs of congestive heart failure appeared or if significant hypotension developed, the dose of propranolol was not increased.

Statistics. Analysis of variance and covariance with repeated measures were used to compare the data between stable and unstable ventricular tachycardia (8). A paired *t* test of repeated measurements was used to compare the changes in sinus rate during ventricular tachycardia (8). In patients in whom multiple episodes of ventricular tachycardia were induced, the mean values were used for comparison. The chi-square test or the Fisher exact test was used to compare the data between the groups. The data are expressed as mean values ± SD.

Results

Clinical data (Table 1). Sixteen patients had 32 episodes of stable induced ventricular tachycardia and 16 patients had 21 episodes of unstable induced ventricular tachycardia. There were no significant differences between the two groups in age, etiology of heart disease, number or location of previous infarctions, number of diseased coronary arteries, cardiac medication or ejection fraction (33 ± 10% in the stable group versus 35 ± 12% in the unstable group). Ventricular fibrillation was more commonly the presenting arrhythmia and cardiac arrest the presenting clinical event in patients with unstable induced tachycardia ($p < 0.05$).

Characteristics of induced ventricular tachycardia (Table 2). The cycle length was longer during stable than unstable ventricular tachycardia, although there was some overlap between the cycle lengths of stable and unstable tachycardia. Four stable ventricular tachycardias had a cycle length ≤250 ms and four unstable tachycardias had a cycle length >250 ms. Six unstable tachycardias degenerated to ventricular fibrillation before termination of arrhythmia. Twenty-seven tachycardias were terminated by countershock, six of which required more than one shock.

Changes in sinus node rate during induced ventricular tachycardia. Sinus node cycle lengths were measured before ventricular tachycardia and at 5 s intervals until termination of stable (Fig. 1) and unstable (Fig. 2) tachycardias (Fig. 3).

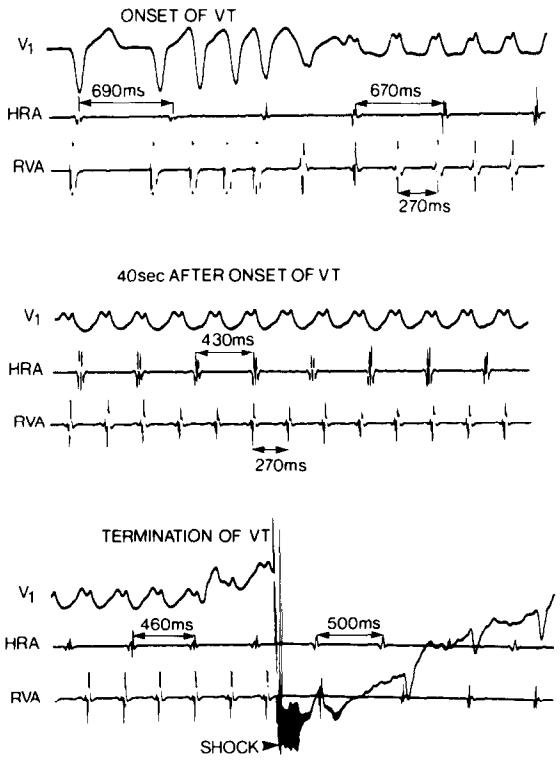
Table 2. Characteristics of 53 Induced Ventricular Tachycardias in 32 Patients

	Stable VT (n = 32)	Unstable VT (n = 21)
Mode of termination of VT/VF		
Spontaneous	3 (9%)	0
Pacing	23 (72%)	0
Countershock	6 (19%)	21 (100%)
Degeneration of VT to VF	0	6 (29%)
Cycle length of VT (ms)	320 ± 62	235 ± 51*
Duration of VT (s)	62 ± 36	34 ± 7*

*$p < 0.05$ between the groups. VF = ventricular fibrillation; other abbreviations as in Table 1.

During stable tachycardia, the sinus rate increased from 85 ± 10 impulses/min to a maximum of 109 ± 12 impulses/min ($p < 0.001$), and did not decrease significantly before termination of tachycardia (102 ± 15 after termination). During unstable tachycardia, the sinus rate increased from 82 ± 12 beats/min to a maximum of 104 ± 14 beats/min ($p < 0.001$). However, during unstable tachycardia, the sinus rate began to decrease 5 to 30 s (mean 13 ± 8 s) after onset of

Figure 1. Recordings of sinus node activity and ventricular activity from one surface electrocardiogram (lead V_1) and two intracardiac electrograms (HRA = high right atrium, RVA = right ventricular apex) in a patient with stable induced ventricular tachycardia (VT). The rate of sinus node activity increased without significant decrease until termination of ventricular tachycardia.



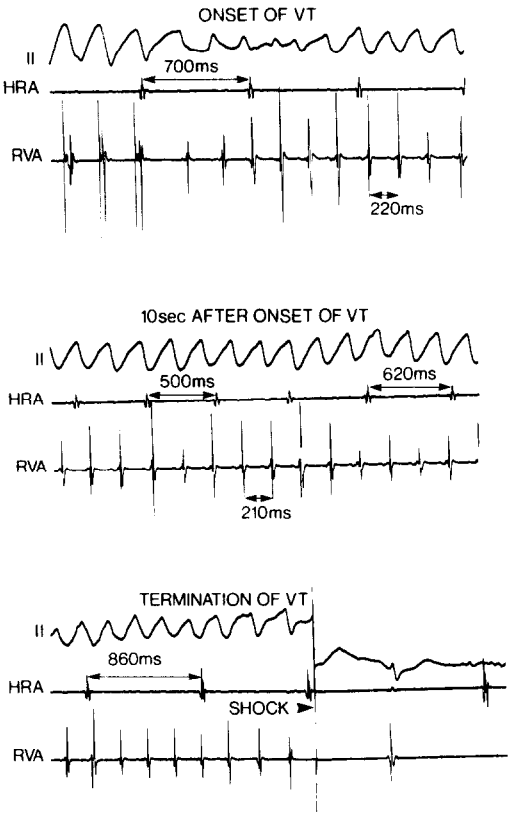
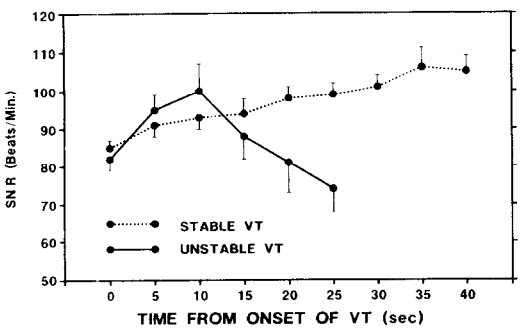


Figure 2. Recordings of sinus node activity and ventricular activity from one surface electrocardiogram (lead II) and two intracardiac electrograms in a patient with an unstable induced ventricular tachycardia (VT). The sinus node cycle length decreased initially after induction of ventricular tachycardia then increased, but began to decrease 10 s after onset of ventricular tachycardia resulting in slow sinus node activity at termination of tachycardia by countershock. Abbreviations as in Figure 1.

ventricular tachycardia resulting in a slower heart rate after termination (56 ± 15 beats/min) than before ventricular tachycardia ($p < 0.001$). In three of six patients in whom the

Figure 3. Changes in sinus node rate (SNR) as a function of time from onset of sinus tachycardia during 32 episodes of stable ventricular tachycardia (VT) and 21 episodes of unstable ventricular tachycardia. Mean values ± SEM.



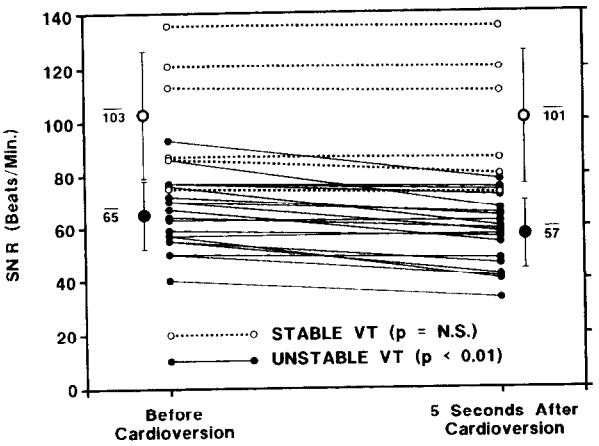


Figure 4. Changes in sinus node rate (SNR) before and 5 s after cardioversion. **Solid lines** represent unstable ventricular tachycardias (VT) and **dotted lines** represent stable ventricular tachycardias. Mean sinus rates are shown for each of four conditions (stable versus unstable, before versus after cardioversion).

unstable ventricular tachycardia degenerated to ventricular fibrillation, the sinus rate started to decrease before ventricular fibrillation. Eight (38%) of 21 patients with unstable induced ventricular tachycardia had marked sinus bradycardia after its termination (<50 beats/min). No patient with stable induced ventricular tachycardia had bradycardia after arrhythmia termination, but sinus tachycardia (>100/min) was noted in 20 (60%) of 32 cases. Sinus rate was 7 ± 6 beats/min slower 5 s after than before defibrillation ($p < 0.001$) (Fig. 4). In six patients with multiple shocks, the sinus rate was 15 ± 3 beats/min slower after termination of tachycardia than before the first shock.

Reproducibility. Ten ventricular tachycardias (six stable and four unstable) were reinduced to the same cycle length (<20 ms difference in cycle lengths). The increase of sinus rate was comparable during each of the two induced tachycardias (from 81 ± 14 to 103 ± 28 impulses/min during the first induction and from 81 ± 15 to 102 ± 30 impulses/min during the reinduced tachycardia [mean difference 5 ± 6 beats/min]). The sinus rates after termination were also comparable (79 ± 18 versus 79 ± 23 beats/min [mean difference 9 ± 10 beats/min]). In four patients whose unstable tachycardia was reinduced at the same cycle length, the same pattern of sinus rate change (i.e., the rapid initial increase with subsequent slowing of sinus rate) was detected in all cases.

Effects of intravenous propranolol (Table 3). Intravenous propranolol was administered to 10 patients at a mean total dose of 11 ± 4 mg (range 6 to 15). In three patients the 15% decrease in sinus node rate was not achieved because of hypotension after propranolol administration. Overall, blood pressure decreased from a mean of 134 ± 12/84 ± 8 mm Hg to 121 ± 14/79 ± 11 mm Hg during propranolol infusion ($p <$ 0.001). The characteristics of ventricular tachycardia before

Table 3. Characteristics of 20 Ventricular Tachycardias Before and After Propranolol

	Before Propranolol (n = 10)	After Propranolol (n = 10)
Mode of termination		
Pacing	4	2
Countershock	6	8
Presentation of VT		
Stable	4	2
Unstable	6	8
Cycle length of VT (ms)	254 ± 63	257 ± 63
Duration of VT (s)	49 ± 33	40 ± 39

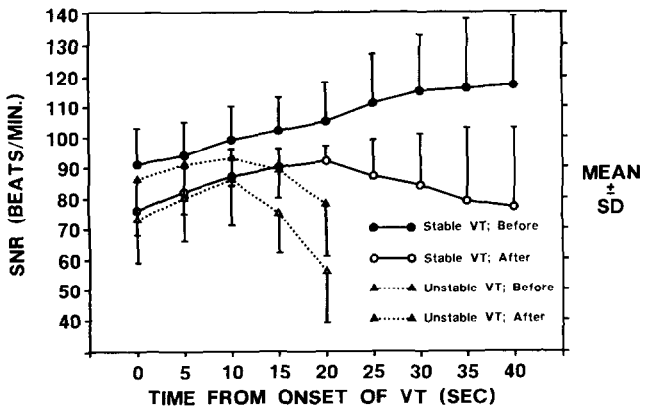
Abbreviations as in Table 1.

and after intravenous propranolol are summarized in Table 3. No significant differences occurred in the cycle length or duration of tachycardia before and after propranolol. Six ventricular tachycardias were unstable and four were stable before propranolol.

Figure 5 displays the changes of sinus rate during ventricular tachycardia before and after propranolol administration. The magnitude of initial increase in sinus rate did not differ before and after beta-adrenergic blockade. The mean increase was 18 ± 6 impulses/min before and 17 ± 7 impulses/min after propranolol (p = NS). During stable ventricular tachycardia, the sinus rate increased from 91 ± 12 impulses/min to a maximum of 117 ± 22 impulses/min ($p < 0.01$) before propranolol. After propranolol, the initial increase in sinus rate (from 76 ± 10 beats/min to 92 ± 5 beats/min, $p = 0.01$) was followed by a decrease in sinus rate (77 ± 26 beats/min at termination).

Two patients with initially stable tachycardia became unconscious and required cardioversion at exactly the same tachycardia cycle length after propranolol. In both patients, the pattern of sinus node rate changes was different after propranolol administration. The initial increase in sinus rate was followed by a decease in sinus rate before termination of ventricular tachycardia after propranolol, whereas sinus rate increased continuously until termination of tachycardia before propranolol. The pattern of sinus rate changes was similar during unstable ventricular tachycardias before and after beta-adrenergic blockade.

Figure 5. Changes in sinus node rate (SNR) during stable and unstable ventricular tachycardias (VT) before and after propranolol administration. See text for details.



Discussion

Increase in sinus rate during ventricular tachycardia. Cardiac autonomic tone may modulate the characteristics of cardiac arrhythmias (1–4), but to our knowledge, only one previous study (4) has evaluated possible mechanisms of changes in cardiac autonomic tone during ventricular tachycardia in humans. In that study, Morady et al. (4) observed only a minimal increase in catecholamine blood levels during tachycardias with a significant increase during the 1st min after countershock for ventricular tachycardia. No data were reported on changes in sinus rate during tachycardia, although it was increased at the time of increased catecholamine blood levels, i.e., 1 min after shock. We observed a significant, reproducible increase in sinus rate during ventricular tachycardia that could reflect changes in cardiac autonomic tone in the absence of sinus node disease or some form of autoregulation (9).

Both increased sympathetic tone and decreased parasympathetic tone could increase spontaneous sinus rate (5–7). The lack of effect of intravenous propranolol on the increase of sinus rate suggests that vagal withdrawal has a greater role than sympathetic activation on sinus rate increase during ventricular tachycardia. This concept is supported by the observations of Morady et al. (4), in which increased plasma catecholamine levels were detected primarily after termination but not during the tachycardia. However, data from both studies may not exclude concomitant sympathetic activation. In fact, a tendency to a blunted increase in sinus rate after beta-adrenergic blockade was noted in two patients with stable induced ventricular tachycardia. Thus, it is possible that the initial increase in sinus rate reflects reduction of vagal tone, whereas the continuous increase during stable tachycardia may be a result of sympathetic activation. A recent experimental study (10) also showed increased sympathetic activity during stable simulated ventricular tachycardia. Furthermore, an earlier study (11) has suggested that vagal withdrawal occurs almost immediately during baroreflex response to hypotension and is later followed by enhancement of sympathetic tone. Studies with both parasympathetic and sympathetic blockade will be required to confirm the relative significance of both vagal and sympathetic reflexes on the observed increase of sinus rate during ventricular tachycardia.

Slowing of sinus rate during unstable ventricular tachycardia. Unstable ventricular tachycardias were accompanied by a significant slowing of the sinus rate, whereas stable

tachycardias resulted in a continuous increase in sinus rate. More than one-third of patients with unstable induced arrhythmia had bradycardia after arrhythmia termination, a finding that concurs with results in earlier studies (12,13). These previous studies reported a higher incidence of sinus tachycardia after cardioversion of induced ventricular arrhythmia. Our exclusion of patients with irregular sinus node activity during ventricular tachyarrhythmia and those with ventricular fibrillation as the initial arrhythmia may explain the lower incidence of sinus tachycardia after cardioversion in our study. The shorter duration of unstable tachycardias due to cardioversion may also influence these observations.

The mechanism of the slowing of sinus rate is not clear. Hemodynamic collapse, high dose energy delivered by cardioversion or ischemia of the sinus node may have a disruptive effect on the intrinsic sinus node function. Sinus node automaticity is also autoregulated during phasic alterations in sinus node artery perfusion (14). Autoregulation may become more compromised during the faster rate and hypotension of ventricular tachycardia. Cardioversion did not appear to be the only factor for the postdefibrillation bradycardia, although it may have augmented the slowing of sinus rate that had started before defibrillation. The association between multiple shocks and postdefibrillation bradycardia observed in this study, as in previous studies (12,13), may be due to both disruptive effects of electrical shocks and longer duration of hemodynamic collapse and loss of consciousness.

The development of bradycardia during unstable ventricular tachycardia may also represent a failure of normal compensation by the baroreceptor mechanisms and may involve either a partial failure of sympathetic activation or an enhancement of vagal tone. Similar mechanisms have been postulated for nitrate syncope associated with bradycardia and have been suggested to be due to decreased central blood volume (15). The contribution of maintenance of sympathetic tone during ventricular tachycardia to its stability is supported by the finding in two patients that the arrhythmia changed from stable to unstable ventricular tachycardia after beta-adrenergic blockade and that bradycardia was augmented after termination of tachyarrhythmia. This view is also supported by experimental data (10) that have shown that beta-adrenergic activation is an important determinant of maintaining the hemodynamic stability during the ventricular tachycardias.

Limitations. The technique used in this study provides information primarily on the balance between sympathetic and parasympathetic activity at the level of the sinus node. Furthermore, it cannot differentiate between autonomic fluctuations and intrinsic sinus node depression as a mechanism of the slowing of heart rate. Despite these limitations, the estimation of changes in sinus rate and the evaluation of the effect of autonomic blockade on the observed changes are currently the only available methods for detecting abrupt changes in cardiac autonomic tone during ventricular tachycardia in humans. Furthermore, although the dose of propranolol may not have been adequate to achieve complete pharmacologic beta-adrenergic blockade (16), even partial beta-blockade would result in significant blunting of sinus rate increase if sympathetic activation were the predominant autonomic mechanism during the initial phase of ventricular tachycardia.

Conclusions. Previous studies (17,18) have documented a relation between slow heart rate after defibrillation and poor prognosis in patients resuscitated from out-of-hospital cardiac arrest. It has been postulated (18) that the time from onset of malignant arrhythmia to defibrillation might be the reason for bradycardia as a presenting rhythm after cardioversion. Another study (12) proposed that defibrillation itself caused sinus bradycardia after termination of ventricular tachycardia. The present data show that the slowing of heart rate starts quickly after a brief increase in sinus rate during unstable ventricular tachycardias, whereas stable ventricular tachycardia results in sinus tachycardia. Thus bradycardia after defibrillation may be related to the characteristics of the initial arrhythmia in addition to the duration of ventricular tachycardia and the disruptive effect of cardioversion.

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